

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-26 (Canceled)

27. (Previously presented) A method for evaluating a binding property of a polynucleotide probe to a target nucleotide sequence, said polynucleotide probe comprising a predetermined nucleotide base sequence that is complementary to at least a hybridizable portion of said target nucleotide sequence, said method comprising determining a ratio of the amount of hybridization of polynucleotides in a first sample to the polynucleotide probe and the amount of hybridization of polynucleotides in a second sample to the polynucleotide probe, wherein:

- (a) the first sample comprises a plurality of polynucleotide molecules comprising said target nucleotide sequence; and
- (b) the second sample comprises a plurality of different polynucleotide molecules wherein each different polynucleotide molecule comprises a sequence that is different from the nucleotide sequences of any other polynucleotide molecules in said plurality of different polynucleotide molecules,

wherein at least 75% of the polynucleotide molecules in said first sample are polynucleotide molecules comprising said target nucleotide sequence, and wherein said ratio is used as a measure of said binding property, thereby evaluating said binding property of said polynucleotide probe.

28. (Canceled).

29. (Currently amended) The method of claim 27 wherein the target ~~polynucleotide~~ nucleotide sequence in the first sample is a nucleotide sequence from a gene or gene transcript of a cell or organism, or of an mRNA, cDNA or cRNA derived therefrom.

30. (Currently amended) The method of claim 27 wherein the plurality of different polynucleotide molecules in the second sample ~~comprise~~ comprises nucleotide sequences from a plurality of genes or gene transcripts of a cell or organism.

Claims 31-32 (Canceled)

33. (Previously presented) The method of claim 27 wherein at least 90% of the polynucleotide molecules in said first sample are said polynucleotide molecules comprising said target nucleotide sequence.

34. (Previously presented) The method of claim 33 wherein at least 95% of the polynucleotide molecules in said first sample are said polynucleotide molecules comprising said target nucleotide sequence.

35. (Previously presented) The method of claim 34 wherein at least 99% of the polynucleotide molecules in said first sample are said polynucleotide molecules comprising said target nucleotide sequence.

36. (Previously presented) The method of claim 27 wherein each different polynucleotide molecule in the second sample does not comprise the target nucleotide sequence.

37. (Currently amended) The method of claim 36 wherein:

- (a) the target ~~polynucleotide~~ nucleotide sequence in the first sample is a sequence from a gene or gene transcript of a cell or organism; and
- (b) the second sample comprises a polynucleotide sample from a deletion mutant of the cell or organism,

wherein the deletion mutant of the cell or organism does not express the gene or gene transcript.

38. (Previously presented) The method of claim 27 wherein the plurality of different polynucleotide molecules in the second sample comprises:

- (a) polynucleotide molecules comprising the target nucleotide sequence, and
- (b) a plurality of different polynucleotide molecules, each comprising a different nucleotide sequence and each not comprising the target nucleotide sequence.

39. (Currently amended) The method of claim 38 wherein:

- (a) the target nucleotide sequence ~~comprises~~ is a sequence from a gene or gene transcript of a cell or organism; and
- (b) the second sample comprises a polynucleotide sample from a wild-type strain of the cell or organism,

wherein the wild-type strain of the cell or organism expresses the gene or gene transcript.

40. (Previously presented) The method of claim 27 wherein:

- (a) the first sample further comprises polynucleotide molecules that do not comprise the target nucleotide sequence; and
- (b) the second sample lacks said polynucleotide molecules comprising said target nucleotide sequence.

41. (Canceled)

42. (Previously presented) The method of claim 40 wherein:

- (a) the target nucleotide sequence is a sequence from a gene or gene transcript of a cell or organism;
- (b) the first sample comprises a polynucleotide sample from a wild-type strain of the cell or organism which expresses the gene or gene transcript; and
- (c) the second sample comprises a polynucleotide sample from a deletion mutant of the cell or organism which does not express the gene or gene transcript.

43. (Previously presented) The method of claim 27 wherein

- (a) the first sample further comprises polynucleotide molecules that do not comprise the target nucleotide sequence; and
- (b) the second sample comprises:
 - (i) polynucleotide molecules comprising the target nucleotide sequence, and
 - (ii) a plurality of different polynucleotide molecules, each different polynucleotide molecule comprising a different nucleotide sequence and not comprising the target nucleotide sequence,

wherein the amount of polynucleotide molecules in the first sample comprising the target nucleotide sequence differs by at least a factor of two from the amount of polynucleotide molecules in the second sample comprising the target nucleotide sequence.

44. (Previously presented) The method of claim 43 wherein the amount of polynucleotide molecules in the first sample comprising the target nucleotide sequence differs from the amount of polynucleotide molecules in the second sample comprising the target nucleotide sequence by at least a factor of four.

45. (Previously presented) The method of claim 43 wherein the amount of polynucleotide molecules in the first sample comprising the target nucleotide sequence differs from the amount of polynucleotide molecules in the second sample comprising the target nucleotide sequence by at least a factor of eight.

46. (Previously presented) The method of claim 43 wherein the amount of polynucleotide molecules in the first sample comprising the target nucleotide sequence differs from the amount of polynucleotide molecules in the second sample comprising the target nucleotide sequence by at least a factor of twenty.

47. (Previously presented) The method of claim 43 wherein the amount of polynucleotide molecules in the first sample comprising the target nucleotide sequence differs from the amount of polynucleotide molecules in the second sample comprising the target nucleotide sequence by at least a factor of 100.

48. (Previously presented) The method of claim 43 wherein each said polynucleotide molecule that does not comprise the target nucleotide sequence in the first sample is present in the second sample in an amount that differs from the amount of said polynucleotide molecule in the first sample by no more than a factor of 100.

49. (Previously presented) The method of claim 43 wherein each said polynucleotide molecule that does not comprise the target nucleotide sequence in the first sample is present in the second sample in an amount that differs from the amount of said polynucleotide molecule in the first sample by no more than a factor of 10.

50. (Previously presented) The method of claim 43 wherein each said polynucleotide molecule that does not comprise the target nucleotide sequence in the first sample is present in the second sample in an amount that differs from the amount of said polynucleotide molecule in the first sample by no more than 50%.

51. (Previously presented) The method of claim 43 wherein the mean abundance of the polynucleotide molecules that do not comprise the target nucleotide sequence in the first sample differs from the mean abundance of the different polynucleotide molecules that do not comprise the target nucleotide sequence in the plurality of different polynucleotide molecules of the second sample by no more than a factor of two.

52. (Previously presented) The method of claim 43 wherein the mean abundance of the polynucleotide molecules that do not comprise the target nucleotide sequence in the first sample differs from the mean abundance of the different polynucleotide molecules that do not comprise the target nucleotide sequence in the plurality of different polynucleotide molecules of the second sample by no more than 50%.

53. (Previously presented) The method of claim 43 wherein the mean abundance of the polynucleotide molecules that do not comprise the target nucleotide sequence in the first sample differs from the mean abundance of the different polynucleotide molecules that do not comprise the target nucleotide sequence in the plurality of different polynucleotide molecules of the second sample by no more than 10%.

54. (Previously presented) The method of claim 43 wherein the mean abundance of the polynucleotide molecules that do not comprise the target nucleotide sequence in the first sample differs from the mean abundance of the different polynucleotide molecules that do not comprise the target nucleotide sequence in the plurality of different polynucleotide molecules of the second sample by no more than 1%.

Claims 55-58 (Canceled)

59. (Previously presented) The method of claim 27 wherein the polynucleotide molecules in the first sample are detectably labeled.

60. (Original) The method of claim 27 wherein the polynucleotide molecules in the second sample are detectably labeled.
61. (Original) The method of claim 59 or 60 wherein the polynucleotide molecules are labeled with a fluorescent molecule.
62. (Previously presented) The method of claim 27 wherein:
- (a) the polynucleotide molecules in the first sample are labeled with a first label;
 - and
 - (b) the polynucleotide molecules in the second sample are labeled with a second label,
- the first label being distinguishable from the second label.
63. (Original) The method of claim 62 wherein:
- the first label is a first fluorescent molecule, and
 - the second label is a second fluorescent molecule.
64. (Original) The method of claim 27 wherein the polynucleotide probe is attached to a surface of a support.
65. (Original) The method of claim 27 wherein the polynucleotide probe is one of a plurality of polynucleotide probes.
66. (Previously presented) The method of claim 65 wherein the plurality of polynucleotide probes comprises polynucleotide probes in an array of polynucleotide probes,
- said array having a support with at least one surface and different polynucleotide probes attached to said surface,
 - wherein each of said different polynucleotide probes attached to said surface is attached to the surface of the support in a different location.
67. (Previously presented) A method for evaluating a binding property of a plurality of polynucleotide probes to a target nucleotide sequence, wherein each polynucleotide probe in the plurality of polynucleotide probes comprises a different predetermined nucleotide base sequence that is complementary to at least a hybridizable portion of said target nucleotide

sequence, said method comprising determining for each said polynucleotide probe a ratio of the amount of hybridization of polynucleotides in a first sample to said polynucleotide probe and the amount of hybridization of polynucleotides in a second sample to said polynucleotide probe, wherein:

- (a) the first sample comprises a plurality of polynucleotide molecules comprising said target nucleotide sequence; and
- (b) the second sample comprises a plurality of different polynucleotide molecules wherein each different polynucleotide molecule comprises a nucleotide sequence that is different from nucleotide sequence of any other polynucleotide molecules in said plurality of different polynucleotide molecules,

wherein at least 75% of the polynucleotide molecules in said first sample are polynucleotide molecules comprising said target nucleotide sequence, and wherein said ratio is used as a measure of said binding property, thereby evaluating said binding property of each said polynucleotide probe.

Claims 68-72 (Canceled).

73. (Original) The method of claim 67 wherein each polynucleotide probe in the plurality of polynucleotide probes is attached to a surface of a support.

74. (Previously presented) The method of claim 67 wherein the plurality of polynucleotide probes comprises polynucleotide probes in an array of probes,

said array having a support with at least one surface and different polynucleotide probes attached to said surface,

wherein each of said different polynucleotide probes attached to said surface in the plurality of probes is attached to the surface of the support in a different location.

75. (Previously presented) The method of claim 67 wherein the first sample comprises two or more different polynucleotide molecules

wherein none of the two or more different polynucleotide molecules hybridizes or cross-hybridizes to a probe that also hybridizes or cross-hybridizes to another one of the two or more different polynucleotide molecules.

Claims 76-83 (Canceled)

84. (Original) The method of claim 27 wherein:

polynucleotides in the first sample are labeled with a first label and polynucleotides in the second sample are labeled with a second label that is distinguishable from the first label; and further comprising, prior to said step of comparing the steps of:

- (i) concurrently contacting the polynucleotide probe with the first sample and the second sample under conditions conducive to hybridization, and
- (ii) detecting any binding that occurs between the polynucleotide probe and polynucleotides in the first sample and the second sample.

85. (Previously presented) The method of claim 84 wherein the second sample lacks polynucleotide molecules of said first sample.

Claims 86-89 (Canceled)

90. (Previously presented) The method of any one of claims 27, 29-30, 33-40, 42-54, 61-67, 73-75 and 84-85, wherein said polynucleotide molecules comprising said target nucleotide sequence are the same polynucleotide molecule.

91. (Previously presented) A method for evaluating a binding property of a plurality of polynucleotide probes to a target nucleotide sequence, said method comprising determining for each said polynucleotide probe a ratio of the amount of hybridization of polynucleotides in a first sample to said polynucleotide probe and the amount of hybridization of polynucleotides in a second sample to said polynucleotide probe, wherein:

- (a) said first sample comprises a plurality of polynucleotide molecules comprising said target nucleotide sequence and a plurality of polynucleotide molecules that do not comprise the target nucleotide sequence; and
- (b) said second sample comprises a plurality of different polynucleotide molecules wherein each different polynucleotide molecule comprises a sequence that is different from the nucleotide sequence of any other polynucleotide molecule in said plurality of different polynucleotide molecules, and wherein each different polynucleotide molecule in the second sample does not comprise the target nucleotide sequence,

wherein each polynucleotide probe in the plurality of polynucleotide probes comprises a different predetermined nucleotide base sequence that is complementary to at least a hybridizable portion of said target nucleotide sequence and wherein said ratio is used as a measure of said binding property, thereby evaluating said binding property of said plurality of polynucleotide probes.

92. (Previously presented) The method of claim 91 wherein:

- (a) said target nucleotide sequence is a sequence from a gene or gene transcript of a cell or organism;
- (b) said first sample comprises a polynucleotide sample from a wild-type strain of the cell or organism which expresses the gene or gene transcript; and
- (c) said second sample comprises a polynucleotide sample from a deletion mutant of the cell or organism that does not express the gene or gene transcript.

93. (Previously presented) A method for evaluating a binding property of a plurality of polynucleotide probes to a target nucleotide sequence, said method comprising determining for each of said polynucleotide probes a ratio of the amount of hybridization of polynucleotides in a first sample to said polynucleotide probe and the amount of hybridization of polynucleotides in a second sample to said polynucleotide probe, wherein:

- (a) said first sample comprises a plurality of polynucleotide molecules comprising said target nucleotide sequence and a plurality of polynucleotide molecules that do not comprise the target nucleotide sequence; and
- (b) said second sample comprises a plurality of different polynucleotide molecules wherein each different polynucleotide molecule comprises a sequence that is different from the nucleotide sequence of any other polynucleotide molecule in said plurality of different polynucleotide molecules,

wherein each polynucleotide probe in the plurality of polynucleotide probes comprises a different predetermined nucleotide base sequence that is complementary to at least a hybridizable portion of said target nucleotide sequence and wherein said ratio is used as a measure of said binding property, thereby comparing said binding property of said plurality of polynucleotide probes.

94. (Previously presented) The method of claim 93 wherein:

- (a) said target nucleotide sequence comprises a sequence from a gene or gene transcript of a cell or organism; and
- (b) said second sample comprises a polynucleotide sample from a wild-type strain of said cell or organism, wherein the wild-type strain of the cell or organism expresses the gene or gene transcript.

95. (Previously presented) The method of claim 93, wherein said second sample comprises:

- (b1) polynucleotide molecules comprising the target nucleotide sequence, and
- (b2) a plurality of different polynucleotide molecules, each different polynucleotide molecule comprising a different nucleotide sequence and not comprising the target nucleotide sequence,

and wherein the amount of polynucleotide molecules in said first sample comprising the target nucleotide sequence differs by at least a factor of two from the amount of polynucleotide molecules in said second sample comprising the target nucleotide sequence.

96. (Previously presented) The method of claim 95 wherein the amount of polynucleotide molecules in said first sample comprising said target nucleotide sequence differs from the amount of polynucleotide molecules in said second sample comprising said target nucleotide sequence by at least a factor of four.

97. (Previously presented) The method of claim 95 wherein the amount of polynucleotide molecules in said first sample comprising said target nucleotide sequence differs from the amount of polynucleotide molecules in said second sample comprising said target nucleotide sequence by at least a factor of eight.

98. (Previously presented) The method of claim 95 wherein the amount of polynucleotide molecules in said first sample comprising said target nucleotide sequence differs from the amount of polynucleotide molecules in said second sample comprising said target nucleotide sequence by at least a factor of twenty.

99. (Previously presented) The method of claim 95 wherein the amount of polynucleotide molecules in said first sample comprising said target nucleotide sequence differs from the

amount of polynucleotide molecules in said second sample comprising said target nucleotide sequence by at least a factor of 100.

100. (Previously presented) The method of claim 95 wherein each said polynucleotide molecule that does not comprise said target nucleotide sequence in said first sample is present in said second sample in an amount that differs from the amount of said polynucleotide molecule in the first sample by no more than 50%.

101. (Previously presented) The method of claim 95 wherein the mean abundance of the polynucleotide molecules that do not comprise the target nucleotide sequence in the first sample differs from the mean abundance of the different polynucleotide molecules that do not comprise the target nucleotide sequence in the plurality of different polynucleotide molecules of the second sample by no more than a factor of two.

102. (Previously presented) The method of claim 95 wherein the mean abundance of the polynucleotide molecules that do not comprise the target nucleotide sequence in the first sample differs from the mean abundance of the different polynucleotide molecules that do not comprise the target nucleotide sequence in the plurality of different polynucleotide molecules of the second sample by no more than 50%.

103. (Previously presented) The method of claim 95 wherein the mean abundance of the polynucleotide molecules that do not comprise the target nucleotide sequence in the first sample differs from the mean abundance of the different polynucleotide molecules that do not comprise the target nucleotide sequence in the plurality of different polynucleotide molecules of the second sample by no more than 10%.

104. (Previously presented) The method of claim 95 wherein the mean abundance of the polynucleotide molecules that do not comprise the target nucleotide sequence in the first sample differs from the mean abundance of the different polynucleotide molecules that do not comprise the target nucleotide sequence in the plurality of different polynucleotide molecules of the second sample by no more than 1%.